May 22, 2003

Richard Henrich
Manager, Regulatory Affairs
Great Lakes Chemical Corporation
Highway 52 N.W.
West Lafayette, IN 47996

Dear Mr. Henrich:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 1,2-bis(2,4,6-tribromophenoxy)ethane posted on the ChemRTK HPV Challenge Program Web site on January 23, 2003. I commend Great Lakes Chemical Corporation for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Great Lakes Chemical Corporation advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: A. Abramson
W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
1,2-Bis(2,4,6-tribromophenoxy)ethane

Summary of EPA Comments

The sponsor, the Great Lakes Chemical Corporation (GLCC), submitted a test plan and robust summaries to EPA for 1,2-bis(2,4,6-tribromophenoxy)ethane (CAS No. 37853-59-1) dated December 11, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 23, 2003.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties and Environmental Fate. Adequate data are available for the purposes of the HPV Challenge Program for all endpoints except water solubility and log Kow. For these two endpoints, the submitter needs to provide additional information to resolve the discrepancies between the measured and estimated values.

2. Health Effects. Adequate data are available for the purposes of the HPV Challenge Program for all endpoints except chromosomal aberrations. EPA recommends that an *in vitro* chromosomal aberrations test be conducted for this endpoint.

3. Ecological Effects. EPA reserves judgement on the type of ecological effects testing that should be conducted until the values for the water solubility and log Kow have been clarified.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the 1,2-bis(2,4,6-Tribromophenoxy)ethane Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility).

Adequate data are available for melting point, boiling point, and vapor pressure. However, the values for water solubility and log Kow need to be clarified.

Water Solubility. The measured water solubility value is much higher than the value estimated for this chemical using EPIWIN. Because the melting point and chemical structure suggest that the value would be lower than the measured value of 0.2 mg/L, the submitter needs to address this discrepancy.

Partition Coefficient. The submitter states in the Test Plan that "Preference should be given to the measured value" for this endpoint rather than the estimated value. However, the measured log Kow of 3.137 is substantially lower than expected for this compound from its chemical structure, melting point, and from the measured values of two related substances expected to have lower values: tribromophenol (CAS No. 118-79-6; log Kow 4.13) and 1,2-diphenoxyethane (CAS No. 104-66-5; log Kow 3.81). Furthermore, the CLOGP program estimates a log Kow of 8.5 and the KOWWIN program estimates a log Kow of 9.14 for 1,2-bis(2,4,6-tribromophenoxy)ethane.

The submitter needs to resolve this discrepancy. For example, the submitter may wish to conduct another test to measure log Kow. For chemicals expected to have very high log Kows, the slow stirring method is likely to provide a more accurate measurement of log Kow (deBruijn et al, 1989). Because there is only a draft OECD guideline for this method, the submitter should contact EPA for more information.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

Adequate data are available for these endpoints.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Adequate data are available for all endpoints for the purposes of the HPV Challenge Program except chromosomal aberrations.

Genetic Toxicity. The submitter argued against new testing to satisfy the data gap for chromosomal aberrations for four reasons. The submitter's reasons and EPA's responses are as follows: 1) the submitter argued that testing was not necessary because the material was not absorbed well through the gastrointestinal tract; this argument ignores the fact that absorption was sufficient to cause systemic effects (in blood and liver) in the reviewed subchronic feeding assay; 2) the submitter argued against testing because the compound was not expected to cause 'chronic toxicity;' the basis for this assertion is unclear; 3) the submitter asserted that repeated-dose and developmental toxicity studies showed no adverse effects at high doses; this is directly contradicted by the observation of slight anemia and hepatic changes in the reviewed repeated-dose study; and 4) the submitter argued against testing because the testes and ovaries in rats treated in the 106-day feeding bioassay showed no adverse effects. This last point might be suggestive, but is not adequate evidence for establishing the genotoxic potential of the compound. Therefore, the submitter needs to conduct an *in vitro* chromosomal aberrations test to address this endpoint.

Ecological Effects (fish, invertebrates, and algae).

The data presented are inadequate for the purposes of the HPV Challenge Program. The acute fish toxicity test is inadequate because it was performed above the water solubility limit. In addition, the concerns discussed above about the log Kow value raise questions about using estimation for the ecological effects endpoints.

Given the discrepancy between the measured and estimated log Kow values and the possibility that the measured water solubility is too high, EPA reserves judgement on the type of ecological effects testing that should be conducted pending resolution of the water solubility and partition coefficient values. For example, chronic testing may be needed instead of acute testing if the log Kow is determined to be greater than 4.2.

Specific Comments on the Robust Summaries

General

Each summary should clearly identify the test substance by the chemical name. Definitions for some synonyms were provided on page 3 of the test plan. All relevant synonyms (e.g., Firemaster 680), however, should also be added to Section 1.2 of the dossier (page 3 of 51).

Health Effects

Although most studies pre-dated GLP guidelines, the quality of the submitted data and summaries was generally very good. However, none of the original references report the purity of the test article.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

Reference

de Bruijn JHM, Busser F, Seinen W, Hermens J. 1989. Determination of octanol/water partition coefficients with the 'slow-stirring' method. Environ. Toxicol. Chem. 8: 499-512.